



10/760,133.

PTO/SB/21 (07-06)

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<b>TRANSMITTAL FORM</b>  (to be used for all correspondence after initial filing)	Application Number	Patent#: 7,110,889
	Filing Date	Issued: September 19, 2006
	First Named Inventor	Ganesh Venkataraman
	Art Unit	2863
	Examiner Name	T. S. Lau
Total Number of Pages in This Submission	Attorney Docket Number	M0656.70089US01

ENCLOSURES (Check all that apply)		
<input type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input type="checkbox"/> Amendment/Reply <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Reply to Missing Parts/Incomplete Application <input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53	<input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s) _____ <input type="checkbox"/> Landscape Table on CD	<input type="checkbox"/> After Allowance Communication to TC <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input type="checkbox"/> Other Enclosure(s) (please identify below):  <b>Request for Certificate of Correction; Certificate of Correction; copy of pages showing corrections in red</b>
Remarks		

**Certificate of Correction**  
DEC 20 2006

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT			
Firm Name	WOLF, GREENFIELD & SACKS, P.C.		
Signature			
Printed name	Janice A. Vatland		
Date	December 14, 2006	Reg. No.	52,318

Certificate of Mailing Under 37 CFR 1.8(a)	
I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the U.S. Postal Service on the date shown below with sufficient postage as First Class Mail, in an envelope addressed to: ATTN: Certificate of Correction Branch, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.	
Dated: December 14, 2006	Signature:  (Michelle M. Quinn)

DEC 22 2006



Docket No.: M0656.70089US01  
(PATENT)

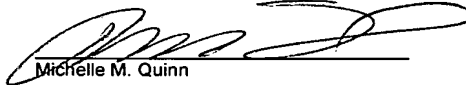
**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Ganesh Venkataraman et al.  
Serial No.: 10/760,133  
Confirmation No.: 7213  
Filed: January 16, 2004  
Patent No.: 7,110,889  
For: METHODS FOR IDENTIFYING AND SEQUENCING POLYMERS  
Examiner: T. S. Lau  
Art Unit: 2863

**Certificate of Mailing Under 37 CFR 1.8(a)**

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Dated: December 14, 2006

  
Michelle M. Quinn

**REQUEST FOR CERTIFICATE OF CORRECTION  
PURSUANT TO 37 CFR 1.322**

Attention: Certificate of Correction Branch  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Upon reviewing the above-identified patent, Patentee noted typographical errors which should be corrected.

In the title:

Please delete "METHOD FOR IDENTIFYING OR CHARACTERIZING PROPERTIES OF POLYMERIC UNITS" and insert --METHODS FOR IDENTIFYING AND SEQUENCING POLYMERS--

In the Claims:

In claim 1, line 15, after polymer, insert -- , wherein the polymer is a polysaccharide --.

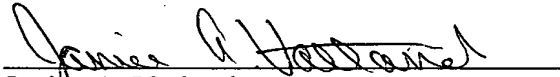
In claim 20, line 19, delete "do no correspond" and insert -- do not correspond --.

DEC 22 2006

The errors were not made on the part of the Applicant, accordingly no fee is believed to be required.

Transmitted herewith is a proposed Certificate of Correction effecting such amendments. Patentee respectfully solicits the granting of the requested Certificate of Correction.

Respectfully submitted,



Janice A. Watland

Registration No.: 52,318

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Date: December 14, 2006  
xndd

DEC 22 2006

**UNITED STATES PATENT AND TRADEMARK OFFICE  
CERTIFICATE OF CORRECTION**

Page 1 of 1

PATENT NO. : 7,110,889  
APPLICATION NO. : 10/760,133  
ISSUE DATE : September 19, 2006  
INVENTOR(S) : Ganesh Venkataraman et al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In the title:

Please delete "METHOD FOR IDENTIFYING OR CHARACTERIZING PROPERTIES OF POLYMERIC UNITS" and insert -- METHODS FOR IDENTIFYING AND SEQUENCING POLYMERS --.

In the Claims:

In claim 1, line 15, after polymer, insert -- , wherein the polymer is a polysaccharide --.

In claim 20, line 19, delete "do no correspond" and insert -- do not correspond --.

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Dated: December 14, 2006

Signature:  (Michelle M. Quinn)

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(12) **United States Patent**  
**Venkataraman et al.**

(10) **Patent No.:** **US 7,110,889 B2**  
(45) **Date of Patent:** **Sep. 19, 2006**

**METHODS FOR IDENTIFYING  
AND SEQUENCING POLYMERS**  
(54) ~~**METHOD FOR IDENTIFYING OR  
CHARACTERIZING PROPERTIES OF  
POLYMERIC UNITS**~~

(75) Inventors: **Ganesh Venkataraman**, Bedford, MA (US); **Zachary Shriver**, Cambridge, MA (US); **Rahul Raman**, Cambridge, MA (US); **Ram Sasisekharan**, Cambridge, MA (US); **Nishla Keiser**, Newton, MA (US)

(73) Assignee: **Massachusetts Institute of Technology**, Cambridge, MA (US)

(\*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **10/760,133**

(22) Filed: **Jan. 16, 2004**

(65) **Prior Publication Data**

US 2004/0197933 A1 Oct. 7, 2004

**Related U.S. Application Data**

(62) Division of application No. 10/356,349, filed on Jan. 31, 2003, which is a division of application No. 09/558,137, filed on Apr. 24, 2000, now Pat. No. 6,597,996.

(60) Provisional application No. 60/159,940, filed on Oct. 14, 1999, provisional application No. 60/159,939, filed on Oct. 14, 1999, provisional application No. 60/130,792, filed on Apr. 23, 1999, and provisional application No. 60/130,747, filed on Apr. 23, 1999.

(51) Int. Cl. **G06F 19/00** (2006.01)

(52) U.S. Cl. **702/27**

(58) Field of Classification Search **702/27**;  
435/6, 183, 10; 526/335, 336; 528/392; 606/228;  
411/373; 530/350; 188/372; 428/343

See application file for complete search history.

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*Primary Examiner*—John Barlow

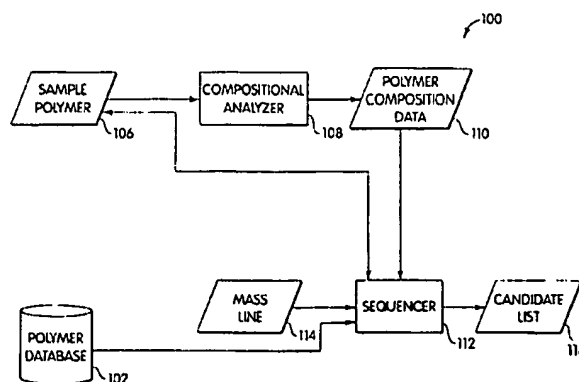
*Assistant Examiner*—Tung Lau

(74) *Attorney, Agent, or Firm*—Wolf, Greenfield & Sacks, P.C.

(57) **ABSTRACT**

The invention relates to methods of identifying and characterizing properties of polymers to provide information about the polymer such as the charge of the polymer, the number and types or characteristics of units of the polymer and the sequence of the polymers. The invention also relates to methods of sequencing polymers such as nucleic acids, polypeptides and polysaccharides and methods for identifying a polysaccharide-protein interaction.

**21 Claims, 13 Drawing Sheets**



DOS, VMS and OS8 are examples, which controls the execution of other computer programs and provides scheduling, debugging, input/output control, accounting, compilation, storage assignment, data management and memory management, and communication control and related services. The processor and operating system define a computer platform for which application programs in high-level programming languages are written.

A memory system typically includes a computer readable and writeable nonvolatile recording medium, of which a magnetic disk, a flash memory and tape are examples. The disk may be removable, known as a floppy disk, or permanent, known as a hard drive. A disk has a number of tracks in which signals are stored, typically in binary form, i.e., a form interpreted as a sequence of one and zeros. Such signals may define an application program to be executed by the microprocessor, or information stored on the disk to be processed by the application program. Typically, in operation, the processor causes data to be read from the nonvolatile recording medium into an integrated circuit memory element, which is typically a volatile, random access memory such as a dynamic random access memory (DRAM) or static memory (SRAM). The integrated circuit memory element allows for faster access to the information by the processor than does the disk. The processor generally manipulates the data within the integrated circuit memory and then copies the data to the disk after processing is completed. A variety of mechanisms are known for managing data movement between the disk and the integrated circuit memory element, and the invention is not limited thereto. It should also be understood that the invention is not limited to a particular memory system.

The invention is not limited to a particular computer platform, particular processor, or particular high-level programming language. Additionally, the computer system may be a multiprocessor computer system or may include multiple computers connected over a computer network. That each module (e.g. 108, 112) in FIG. 1 may be separate modules of a computer program, or may be separate computer programs. Such modules may be operable on separate computers. Data (e.g. 102, 110, 114, 116, and 118) may be stored in a memory system or transmitted between computer systems. The invention is not limited to any particular implementation using software or hardware or firmware, or any combination thereof. The various elements of the system, either individually or in combination, may be implemented as a computer program product tangibly embodied in a machine-readable storage device for execution by a computer processor. Various steps of the process may be performed by a computer processor executing a program tangibly embodied on a computer-readable medium to perform functions by operating on input and generating output. Computer programming languages suitable for implementing such a system include procedural programming languages, object-oriented programming languages, and combinations of the two.

The present invention is not to be limited in scope by examples provided, since the examples are intended as a single illustration of one aspect of the invention. Various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the appended claims. The advantages and objects of the invention are not necessarily encompassed by each embodiment of the invention. All references, patents and patent publications that are recited in this application are incorporated in their entirety herein by reference.

We claim:

1. A method for identifying a subpopulation of polymers having a property in common with a sample polymer of chemical units, comprising:

(A) applying an experimental constraint to the polymer to modify the polymer,

(B) detecting a property of the modified polymer;

(C) identifying a population of polymers of chemical units having the same molecular length as the sample polymer; and

(D) identifying a subpopulation of the identified population of polymers having the same property as the modified polymer by eliminating, from the identified population of polymers, polymers having properties that do not correspond to the modified polymer,

2. The method of claim 1, further comprising repeating steps (A), (B), and (D) on the modified polymer to identify a second subpopulation within the subpopulation of polymers having a second property in common with the twice modified polymer. *wherein the polymer is a polysaccharide.*

3. The method of claim 2, further comprising repeatedly performing the steps (A), (B), and (D) on the modified polymer until the number of polymers within the subpopulation falls below a predetermined threshold.

4. The method of claim 3, wherein the predetermined threshold of polymers within the subpopulation is two polymers and wherein the method is performed to identify the sequence of the polymer.

5. The method of claim 3, wherein the experimental constraints applied to the polymer are different for each repetition.

6. The method of claim 1, wherein the experimental constraint applied to the polymer is digestion with an exoenzyme.

7. The method of claim 1, wherein the experimental constraint applied to the polymer is digestion with an endoenzyme.

8. The method of claim 1, wherein the experimental constraint applied to the polymer is selected from the group consisting of restriction endonuclease digestion; chemical digestion; chemical modification; interaction with a binding compound; chemical peeling; and enzymatic modification.

9. The method of claim 1, wherein the property of the polymer is molecular weight.

10. The method of claim 1, wherein the population of polymers of chemical units includes every polymer sequence having the molecular weight of the sample polymer.

11. The method of claim 1, wherein the population of polymers of chemical units includes less than every polymer sequence having the molecular weight of the sample polymer.

12. The method of claim 1, wherein the step of detection involves the use of mass spectrometry to determine the molecular weight of the polymer.

13. The method of claim 12, wherein the mass spectrometry is matrix assisted laser desorption ionization which detects molecular weight with an accuracy of approximately one Dalton.

14. The method of claim 1, wherein polymer is reduced to at least two fragments and the property of the polymer is the size of the fragments and wherein the step of detection involves strong ion exchange chromatography.

15. The method of claim 1, wherein the step of identifying includes selecting the population of polymers of chemical units from a database including molecular weights of polymers of chemical units.

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16. The method of claim 15, wherein the database includes identifiers corresponding to chemical units of a plurality of polymers, each of the identifiers including a field storing a value corresponding to a property of the corresponding chemical unit.

17. A method for sequencing a polymer, comprising:

(A) applying an experimental constraint to the polymer to modify the polymer,

(B) detecting a property of the modified polymer;

(C) identifying a population of polymers having the same molecular length as the sample polymer and having molecular weights similar to the molecular weight of the sample polymer;

(D) identifying a subpopulation of the identified population of polymers having the same property as the modified polymer by eliminating, from the identified population of polymers, polymers having properties that do not correspond to the modified polymer;

(E) repeating steps (A), (B), and (D) by applying additional experimental constraints to the polymer and identifying additional subpopulations of polymers until the number of polymers within the subpopulation is one and the sequence of the polymer may be identified.

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18. The method of claim 17, wherein the polymer is a polysaccharide.

19. The method of claim 18, wherein the polysaccharide is a heparin-like-glycosaminoglycan.

20. A method for identifying a subpopulation of polysaccharides having a property in common with a sample polysaccharide, comprising:

(A) applying an experimental constraint to the polysaccharide to modify the polysaccharide;

(B) detecting a property of the modified polysaccharide;

(C) identifying a population of polysaccharides having the same molecular length as the sample polysaccharide; and

(D) identifying a subpopulation of the identified population of polysaccharides having the same property as the modified polysaccharide by eliminating, from the identified population of polysaccharides, polysaccharides having properties that do ~~not~~ correspond to the modified polysaccharide.

21. The method of claim 20, wherein the polysaccharide is a heparin-like-glycosaminoglycan.

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